INFLUENCE OF PRESERVATIVES AND OTHER SUBSTANCES ADDED TO FOODS UPON HEALTH AND METABOLISM.

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In connection with studies of food adulteration, which have been conducted during the past twenty-five years under my direction in the Bureau of Chemistry, frequent evidence was obtained of the addition of certain preserving agents and coloring matters to food products. These bodies are not of the character known as condimental; on the contrary, as a rule, they possess neither appreciable taste nor odor in the quantities in which they are employed.

In so far as preservatives are concerned, therefore, the consumer would have no certain knowledge of their presence, and in respect to coloring matters, he would likewise be ordinarily deceived, since such coloring matters are often used to imitate the natural tints found in food products. Thus there would be practiced upon the consumer a fraud in that in the purchase and consumption of foods he was buying and consuming articles which are distinctly not foods and the presence of which is a just cause of suspicion.

The use of chemical preservatives and artificial colors in foods is of quite recent date. I think I may say with safety that if one could go back thirty, or at most, forty years, he would find a food supply practically free, both from chemical preservatives and artificial colors. The rapid development of organic and tinctorial chemistry during the past forty years has made it possible to offer to manufacturers chemical preservatives of high potency, and colors of great beauty and persistence, at prices which make it entirely possible to use them freely in food products. Inasmuch as the use of these bodies, whatever the claims may be in regard thereto, has for its chief purpose either to cheapen the product itself or to sell

it at a higher price than it really should command, it is evident that unless the pecuniary conditions attending the use of these bodies were favorable they would not be employed.

When the claims which are made by manufacturers respecting the use of these substances are carefully considered, we find that most of them are without foundation. In regard to the supposed general preference for artificial color, I would say that an experiment performed on a large number of totally unbiased people has convinced me beyond any reasonable doubt that the great majority of American consumers would prefer uncolored foods. The experiment mentioned was made on about sixty different men during a period of five years to determine whether or not they preferred an artificially colored food or one in its natural tint. Butter, which is perhaps the one food product most universally colored in this country, was used. The subjects on whom the experiment was tried had been in the habit of using nothing except colored butter, hence, if there was any prejudice existing in their minds it must have been in favor of the article which they had constantly consumed. Moreover, the test was made in the winter time when the uncolored butter has the least tint of the whole year, being almost white. No attempt was made to inform the men of the nature of these products. The natural butter and the colored butter were moulded in the same forms and placed upon the same plate, and offered without comment of any kind. At first very few of the men would do more than look at the uncolored butter. A very common expression was, "This is oleomargarine." A few made a trial of its properties. Little by little, without any propaganda of any kind, the whole attitude of these men changed. In the course of four or five months nine tenths of them were using the uncolored butter and they expressed a most decided antipathy to the use of the colored butter when at certain times the supply of the uncolored butter was exhausted.

I believe that this completely refutes the arguments of those who claim that they color butter to meet the demand of the consumer. In point of fact, the color in butter has been almost from the first a fraudulent process. It is a common belief that the best butter of the year is produced during the early spring months, and especially

in June, when the cows have access to the succulent pastures. During this time, owing to the oxidation of the chlorophyll of the grass, a xanthophyll is produced, imparting to the cream a rich golden, or yellow, tint which is, of course, perpetuated in the butter. During the winter months, when the chlorophyll is withdrawn practically from the diet of the cow, this natural coloring matter is absent. The use of the artificial color, therefore, is to simulate for winter butter the color of the butter in June, and thus to conceal what is at least believed to be inferiority.

Again, in experimental observations of a less extended character, I have found that the American consumer does not prefer his foods preserved with chemical preservatives. In a large number of instances which have come under my own personal observation the consumer has stopped eating an article as soon as he has found that it contains a chemical powerful enough to inhibit fermentative action. The users of chemical preservatives, however, do not as a rule claim that they use them at the demand of the consumer. A careful study of manufacturing data made by one of the most conscientious manufacturers in the West shows that it costs more to make a food product without a preservative than it does with a preservative. In very extensive practical experiments on tomatoes this manufacturer found that it was necessary to charge from fifteen to twenty cents more for ketchup per case made without a preservative than with a preservative. Thus I think it is well established by this experimental study that the real reason which the manufacturers have for using chemical preservatives is to cheapen the cost of production. This of itself would be a most worthy object, because presumably the cheapening of the cost of production would lower the price to the consumer. If, therefore, a food product of equal nutritive value and equal wholesomeness could be produced with the aid of chemical preservatives, such a process should meet with the approbation of all. But a very serious problem of a different kind is presented here. A chemical preservative is effective usually by reason of its inhibitive action on fermentation. Very extensive studies of this action of chemical preservatives have led to the general conclusion that while these bodies inhibit the fermentative action giving rise to the ordinary

evidences of decay and putrefaction, and, as a rule, stop most effectively those fermentations which produce alcohol and carbon dioxid, they do not have the same restrictive influence on those processes resulting in the general degradation and decay of organic matter, due chiefly to that class of chemical reactions which is represented by the term hydrolysis. In other words, the ferments which break down, for instance, nitrogeneous tissues into more soluble and finally more dangerous forms of combination, are not so particularly inhibited as is the first class of ferments mentioned.

This fact might well be used, however, as a justification of the employment of chemical preservatives, since if they prevent the ordinary processes of fermentation which produce evident indications of decay and putrefaction, it might be held that they would not interfere with that other class of fermentations or hydrolytic processes peculiarly exercised by the digestive ferments. It will probably not be contested at the present time that there is some justification for this plea, since it has been well established that an amount of a preservative which will for instance prevent alcoholic fermentation will not interfere in anything like so serious a manner with the action of such ferments as the diastatic ferments of the saliva, of the stomach, and of the pancreas. On the other hand, it is well established that in any notable quantities these preservatives do interfere with even the latter class of ferments.

But the problem which is of most importance in this connection is, What is the chief effect of these preservatives upon the health of those who constantly use them and upon the metabolism resulting from the normal functions of the body? To answer this question, there was begun in an experimental way in the Bureau of Chemistry, under my direction, a few years ago, a series of studies having for their purpose the elucidation of this problem. The general plan of the experimental work was extremely simple. It contemplated the selection of a number of young men between the ages of twenty and thirty, in excellent health, who had suffered from no serious disease in the immediate past, who were of steady habits, who were not addicted to the use of alcohol, and whose character was such as to warrant especial confidence and trust in their veracity and general conduct. Such young men evidently are to be

found among those who pass the examinations for the civil service of the United States. In these examinations the very qualities which were looked for in the young men in question must be present or they could not receive the vouchers for character and conduct which are necessary to entitle them to compete in the examinations. These young men were subjected to a careful physical examination similar to that exercised upon those who apply for policies in life insurance companies. This examination showed them free from organic diseases and not to have suffered within a year, usually not at all, from any serious disturbance of health. The subjects were placed upon their honor, by a formal pledge, that they would obey all the rules established for the experimental work and abstain from any form of food and drink except that offered in the regular course of the investigation. Those who used tobacco, tea and coffee were permitted to continue to do so in the regular manner so as not to change the habits of their previous daily life. They were also limited by their pledge to a regular course of exercise which they undertook to follow without variation, and also regular hours of work and sleep. As a justification of the faith and confidence reposed in these young men I think it is sufficient to say that, although during the five years of the experiments we have had about sixty young men under observation, only three have been found to have violated their pledges.

The subjects so selected were first placed on a generous diet of the kind and character to keep them in equilibrium; that is, to maintain the weight of their body without notable changes. The part of the experiment devoted to this purpose was known as the "fore period." Each one was allowed to determine, within certain limits, the character of the diet from the foods offered; that is, a relative amount of meat, bread, potatoes, butter, milk, coffee, tea, etc., to suit his taste and to conform with his previous habit of life. Only in those cases where an excess of some particular kind of food seemed to be preferred was any restriction placed upon this matter. This fore period, therefore, enabled us to determine the magnitude of the ration which would preserve the body equilibrium and presumably be in entire conformity with the normal digestive functions.

The study of the food ingested and of the excreta secured established a chemical control whereby it would be easy to determine any variation in the quantity of food consumed should any of the young men attempt to evade the conditions of their pledge. Having thus established the normal conditions of the body and ascertained the normal metabolic processes, there was introduced into the same ration varying quantities of the preservative which was to be studied. It was thus evident that any change taking place in health or metabolism could be due only to the one factor which was varied in the method of life, namely the injection of the chemical preservative. This period, during which a drug was used, was known as the "preservative period," and lasted, according to circumstances, from twenty to sixty days, depending upon the character and magnitude of the effects produced. As soon as any decided disturbance of health was produced, clearly traceable to the administration of the preservative, its future use was discontinued since it was not the purpose to seriously or permanently affect the health of the subject, but only to secure positive diagnostic data. Then followed an "after period," during which the chemical, or drug, was withdrawn from the food and the normal ration continued as in the fore period, the object being to correct, if possible, any disturbances of metabolism which had been produced and restore the subject again to normal conditions of health and digestion and also to study the after effects of the preservative should such persist. This period of observation was called the "after period." Thus each series of experimental investigations were divided into these three periods.

During the progress of the experiment the following substances were added to the foods for the purposes mentioned above: Boric acid, borates, salicylic acid, salicylates, benzoic acid, benzoates, sulphurous acid, sulphites, formaldehyde, sulphate of copper and potassium nitrate. There is given in the accompanying table a condensed statement of the effects which were produced in these various cases. It is not the purpose of this paper to go into the experimental detail of this matter. The amount of chemical analysis incident to this study was enormous. A great many chemists gave their entire time during the whole period of observation to these analytical problems,

HEALTH AND METABOLISM AS INFLUENCED BY PRESERVATIVES.[1]

Administration of Preservatives.				Medical and Clinical Notes.	Body Weight	Urine Determinations.				Red Blood Corpuscles.	Metabolism.		(Percentage of Total Excretion.)		
Substance.	Number of Days.	Daily Amount Grams.	Total (Maximum). Grams.			Volume.	Albumin.	Acidity.	Microscopic Bodies.		Nitrogen.	Phosphoric Acid.	Sulphur.	Fat.	Solids.
Borax	(3 series)	0.5–3.0	79.5 (minimum 13)	Loss of appetite, nausea, headache, depression	—	o	—	+	o	o	—	+	.....	o	+ (very small)
Boric acid	30 to 70	0.5–5.0			—	o	+	+	o	o					
Salicylic acid and salicylates	30	0.21–2	30.85	Hunger, slight headache, and abdominal pain; symptoms not general.	—	o	o (Special study)	o (Special study +)	+	+	Total — (slight) Urine +	—	—	—	Total — Urine+
Sulphurous acid	20	0.171 –0.4	6.856	Headache, dizziness, pain in stomach; weakness; depression.	o	+ (more marked)	+ (slight)	+	+	— (very marked)	+ (especially in feces)	Total + Urine —	Total + Feces—	+ (very slight)	+
Sodium sulphite		0.223 –0.762	12.565		—	+	+ (slight)	+ (more marked)		— (very marked)	+ (especially in feces)	Total + Urine —	Total + Feces—	+ (very slight)	+
Benzoic acid	20	1–2.5	35[2]	Nausea, headache, lassitude.	—	— (slight)	.....	.....	+ (slight)	— +	+	+	+	— (very slight)	+ (very slight)
Benzoates					—	— (slight)									
Formaldehyde	15	0.1–0.2	2.5	Headache, abdominal pains; sometimes nausea and rash.	—	+	o (+ very few cases)	o (— very few cases)	+ (very slight)	— (not conclusive)	—	Total + Feces —	—	— (very slight)	Total — Urine+
Copper sulphate	19	0.05 –0.15	1.9	Pains in stomach and abdomen; nausea, indigestion; headache; nervousness.	— (very slight)	o	o	o	+ (slight)	—	Total — (Feces +)	— (marked)	Total o (Feces —)	— (slight)	—
Potassium nitrate	60	0.15 –.60	12	Slight headache, pains in epigastrium.	— (slight)	— (Summer)	o	+	+	+	—	— (marked)	+ (slight)	.....	.....

[1] Plus sign signifies a gain, minus sign a loss, and zero practically no change in the preservative period as compared with the fore period.

[2] Only three subjects took the maximum amount.

and in addition to that a number of calculators were employed to tabulate, classify, and average the data. The experimental data which were obtained are published in Bureau of Chemistry Bulletin 84, which when completed will contain the entire series of studies. Part I, of Bulletin 84, is devoted to the detailed study of the effect of borates and boric acid upon health and metabolism. This part of the Bulletin consists of 477 pages. Part II is devoted to the study of salicylic acid and salicylates and contains 283 pages. Part III contains the data relating to sulphurous acid and sulphites, and contain 281 pages, making a total of published matter of 1,041 pages.

CHANGES IN THE URINARY NITROGEN AND SULPHUR COMPOUNDS.[1]

Preservative.	Dose. [Grams per Day.]	Urea.	Uric Acid.	Kreatinin.	Ammonia.	Xanthin.	Neutral.	Total Sulphates.	Inorganic Sulphates.	Ethereal Sulphates.
Borax	0.5 -3.0	.....	.....	.....	.....	.....	.....	.....	.....	.....
Boric acid	0.5 -5.0	.....	.....	.....	.....	.....	.....	.....	.....	.....
Salicylic acid and salicylates	0.21-2.0	—	—	+	—	o	+	+	+	+
Sulphurous acid	0.17-0.4	—	—	o	—	o	+	+	+	+
Sulphites	0.22-0.76	—	—	o	—	o	+	+	+	o
Benzoic acid	1.0 -2.5	.....	.....	.....	.....	.....	—	+	+	o
Benzoates	1.0 -2.5	.....	.....	.....	.....	.....	—	+	+	o
Formaldehyde	0.1 -0.2	—	.....	.....	.....	.....	o	o	o	o
Copper sulphate	0.05-0.15	—	+	.....	.....	+	+	—	o	—
Potassium nitrate	0.15-0.6	—	o	o	—	.....	—	o	+	o

The data relating to benzoic acid and benzoates are in press. These data, together with those relating to the other parts of the study which have been completed and submitted for publication, will make a volume of approximately 2,100 pages. All that I can give in this paper will be the general conclusions relating to each part of the study.

CONCLUSIONS.

Boric Acid and Borates.—In the consideration of the action of preservatives of a mineral nature, such as borax and boric acid, it must be remembered that the animal as well as the plant possesses

[1] Minus and plus signs indicate decreased or increased total excretion in preservative period as compared with the fore period.

a certain mineral hunger. In other words, mineral substances play a double role in animal and plant nutrition: First, they may serve as real foods, necessary to the formation and nutrition of the tissue. In the animal economy this is especially true of phosphoric acid and lime. In the second place, they are necessary to the functional activity of the various organs of the body, irrespective of any part they may take in direct nutrition.

The necessity of saline solutions in the blood is known to every physician and physiologist. If the blood were deprived of all of its saline constituents the circulation would be impeded, restricted, or stopped, and death would result. In cases of collapse in disease saline injections in the blood are often used as a restorative measure. These salts in solution stimulate the heart's action and undoubtedly are active in the osmotic operations of the cells. This is one of the facts which show the intimate relation existing between physical chemistry and physiology.

Common salt is the most frequent and most abundant of the saline constituents of the blood, but the alkalinity of the blood is not due of course to the common salt, which is a neutral substance. The existence of alkaline carbonates or other alkaline salts is necessary to the vital functions. While it is true that the digestion in the stomach takes place in an acid solution, it is likewise true that any excessive acid must be neutralized and enough of alkali added in the small intestine in order that the further digestion of the food may properly take place. That saline bodies other than common salt or the alkaline carbonates may be useful, however, in the performance of the vital functions cannot be denied, though it might be difficult to demonstrate their absolute necessity. Hence the introduction of saline bodies, which may or may not be of an antiseptic character, may, within certain limits, have a favorable influence upon health and digestion. At the same time it should not be forgotten that all excess of such bodies imposes upon the excretory organs an additional burden, which, while it might not impair their efficiency even for a number of years, might finally produce a condition of exhaustion which would be followed by serious consequences. Especially is this remark true of the kidneys, which appear to be a

general clearing house for all the surplus of saline matters, ingested in the foods.

The most interesting of the observations which were made during the progress of the experiments was in the study of the direct effect of boric acid and borax, when administered in food, upon the health and digestion. When boric acid, or its equivalent in borax, is taken into the food in small quantities, not exceeding half a gram ($7\frac{1}{2}$ grains) a day, no notable effects are immediately produced. The medical symptoms of the cases, in long-continued exhibitions of small doses or in large doses extending over a shorter period, show in many instances a manifest tendency to diminish the appetite and to produce a feeling of fullness and uneasiness in the stomach, which in some cases results in nausea, with a very general tendency to produce a sense of fullness in the head, which is often manifested as a dull and persistent headache. In addition to the uneasiness produced in the region of the stomach there appear in some instances sharp and well-located pains, which, however, are not persistent. Although the depression in the weight of the body and some of the other symptoms produced persist in the after periods, there is a uniform tendency manifested after the withdrawal of the preservative toward the removal of the unpleasant sensations in the stomach and head above mentioned.

The administration of boric acid to the amount of 4 or 5 grams per day, or borax equivalent thereto continued for some time, results in most cases in loss of appetite and inability to perform work of any kind. In many cases the person becomes ill and unfit for duty. Four grams per day may be regarded, then, as the limit of exhibition beyond which the normal man may not go. The administration of 3 grams per day produced the same symptoms in many cases, although it appeared that a majority of the men under observation were able to take 3 grams a day for a somewhat protracted period and still perform their duties. They commonly felt injurious effects from the dose, however, and it is certain that the normal man could not long continue to receive 3 grams per day.

In many cases the same results, though less marked, follow the administration of borax to the extent of 2 grams and even of 1 gram per day, although the illness following the administration of

borax and boric acid in those proportions may be explained in some cases by other causes, chiefly grippe.

The administration of borax and boric acid to the extent of one half gram per day yielded results markedly different from those obtained with larger quantities of the preservatives. This experiment, Series V, conducted as it was for a period of fifty days, was a rather severe test, and it appeared that in some instances a somewhat unfavorable result attended it. On the whole, the results show that one half gram per day is too much for the normal man to receive regularly. On the other hand, it is evident that the normal man can receive one half gram per day of boric acid, or of borax expressed in terms of boric acid, for a limited period of time without much danger of impairment of health.

It is, of course, not to be denied that both borax and boric acid are recognized as valuable remedies in medicine. There are certain diseases in which these remedies are regularly prescribed for both internal and external use. The value which they possess in these cases does not seem to have any relation to their use in the healthy organism except when properly prescribed as prophylactics. The fact that any remedy is useful in disease does not appear to logically warrant its use at any other time.

It appears, therefore, that both boric acid and borax, when continually administered in small doses for a long period or when given in large quantities for a short period, create disturbances of appetite, of digestion, and of health.

Salicylic Acid and Salicylates.—In the conclusions based upon the general observations the same conservatism must be observed and the same general reservations made as are found in Part I concerning boric acid and borax. While, as described in the borax report, the attempt has been made to control as far as possible, all the conditions of the experimental work, the difficulties attending the task are so enormous that it is not possible that complete success should be secured. There has, however, been no attempt made to discriminate in the choice of data, all the observations being recorded and the discussion of the individual data based upon the tabular statements being without prejudice and without bias. The general assumption has been made, as in the previous cases, that,

by reason of the regular habits of life which were imposed upon the subjects, the amount of energy developed and the quantity of nourishment expended therein are reasonably constant throughout the experimental period. If these factors vary, as they necessarily must to a certain degree, it is evident that they vary uniformly above or below the average, and hence these variations could not possibly produce any notable effect upon the final result.

There has been a general consensus of opinion among scientific men, including the medical profession, that salicylic acid and its compounds are very harmful substances, and the prejudice against this particular form of preservative is perhaps greater than against any other material used for preserving foods. This is due not only to the belief in the injurious character of salicylic acid, but perhaps is especially due to the fact that it has in the past been so generally used as an antiseptic. That salicylic acid should be singled out especially for condemnation among preservatives does not seem to be justified by the data which are presented and discussed in this bulletin. That it is a harmful substance, however, seems to be well established by the data taken as a whole, but it appears to be a harmful substance of less virulence than has been generally supposed. There is no doubt of the fact that salicylic acid is a drug which is often indicated in diseases well established and also perhaps in certain conditions which, while verging on disease, might still be regarded as a state of health. But the administration of salicylic acid as a medicine should be controlled exclusively by the medical profession, and while it is a remedy well established in the Pharmacopœia and especially prized for its effect upon rheumatism and gout, it does not seem that there should be any warrant in this fact for its promiscuous use in foods, even if it were harmless.

The data show very clearly that salicylic acid and salicylates appear to exert an exciting influence upon the activities which take place in the alimentary canal, stimulating the organs to greater effort, and this stimulation leads at first to increased solubility and absorption of the foods which are introduced into the stomach. In the light of the data which are exhibited salicylic acid may be said to increase the solubility and absorption of the food in the alimentary

canal, so that larger parts of the nutrients taken into the stomach actually enter the circulation.

The data which show the effect just noted also indicate that the general effect upon the system is depressing, in that the tissues are broken down more rapidly than they are built up, and thus the normal metabolic processes are interfered with in a harmful way. The administration of the salicylic acid is attended by a gradual decrease in the weight of the subjects, although the quantity of food elements administered during the preservative and after periods is slightly increased, which fact, together with the greater degree of absorption of the food elements, should have resulted in a slight increase in weight. This increase in weight, however, does not occur, and the disturbing influence of the salicylic acid upon metabolism, although not very great, is specifically demonstrated.

The final conclusion in this matter, therefore, is that the unenviable position which salicylic acid has heretofore held among preservatives, in being regarded as the most injurious of all, is to a certain extent undeserved. Like other ordinary preservatives, it is not one which can be classed as a poison in the usual sense of the word. When used as a medicine in many cases of derangement of health it is like the other chemical preservatives, often highly beneficial when properly prescribed by a competent physician. It is when used in the food at first an apparent stimulant, increasing the absorption and solubility of the common food elements from the alimentary canal. It soon, however, loses its stimulating properties and becomes a depressant, tending to break down the tissues of the body more rapidly than they are built up. It disturbs the metabolic processes, in most cases producing conditions which are not normal and which, apparently, are not beneficial. It has a tendency to diminish the weight of the body and to produce a feeling of discomfort and malaise, which, while not marked, is distinctly indicative of injury. In some cases these symptoms of malaise approach illness, and while not always diagnostic are sufficiently common to point unmistakably to the salicylic acid as their origin. It places upon the excretory organs, especially the kidneys, an additional burden which they are not able to bear and which cannot possibly result in any good, but on the contrary must necessarily finally result in injury, though per-

haps with the use of very small quantities of the preservative these organs would continue to perform their function for many years before finally breaking down.

This work is offered as an unbiased study of all the data recorded, both of those which appear to be in favor of the use of salicylic acid and those which appear to be against its use, and leads to the inevitable conclusion that salicylic acid is a substance which, when added to foods even in small quantities, exerts a depressing and harmful influence upon the digestion and health and the general metabolic activities of the body. Further, there appears to be no necessity for its use, as food can be preserved in unobjectionable ways without its aid. Its indiscriminate use would tend to carelessness in the quantities employed, thus increasing the dangers to which the consumer is subjected. Also its use in the preservation of foods tends to induce carelessness and indifference on the part of the manufacturer, as when a chemical antiseptic is employed many of the processes necessary to the proper selection, cleaning, and preservation of foods may be omitted.

The addition of salicylic acid and salicylates to foods is therefore a process which is reprehensible in every respect, and leads to injury to the consumer, which, though in many cases not easily measured, must finally be productive of great harm.

Sulphurous Acid and Sulphites.—From a careful consideration of the data in the individual cases and the summaries of the results, it appears that the administration of sulphurous acid in foods, either in the form of sulphurous acid gas in solution or in the form of sulphites, is objectionable and produces serious disturbances of the metabolic functions and injury to health and digestion. This injury manifests itself in a number of different ways, both in the production of clinical symptoms which indicate serious disturbances, malaise, or positive suffering, and also by inducing certain changes in the metabolic processes which are not manifested in the way of ordinary clinical symptoms, and are only detected by careful chemical and microscopical study of the excretory products. It can safely be said from the evidence adduced that the administration of sodium sulphite and sulphurous acid as above indicated produces a marked influence of an unfavorable character on metabolism. As

a result of this action an assimilation of food materials containing organic phosphorus is retarded, while there is evidence of increased sulphur katabolism. The sulphur balance sheets show what an immense burden has been added to the already overworked kidneys, which are called upon in this case to remove nearly all, if not quite all, of the added sulphur from the body, previously converted, in great part to sulphuric acid. It is not possible that placing upon the kidneys this increased work of excreting sulphur can result in anything but injury. The fact that the microscopic crystalline and amorphous bodies in the urine are increased in number under the influence of the added sulphur, is another indication of the extraordinary demands made upon the kidneys in such circumstances.

This increase is interesting in respect of the effect which the continued exhibition of sulphurous acid must eventually have upon the structure of the kidney. It is reasonable to suppose that the continued use of a body which produces such results would cause lesions of a histological character which eventually would develop conditions which would give serious apprehension. In the nature of these experiments it was not possible to examine the organs of the body histologically and hence the above conclusion is only based upon experience of a similar character where the organs in question have been subject to such examinations. While there might be no distinguishable lesion of the kidneys produced during a period of twenty or thirty days, or even longer, it is plain that sooner or later lesions of a very serious character producing organic diseases, possibly of an incurable type, would be induced. The further observation that there is a marked tendency to the production of albuminuria, although of an incipient character, is an indication of the unfavorable results of the administration of the sulphurous acid. It is, therefore, evident that by increasing the burden upon the excretory organs, the administration of sulphur in the form mentioned is highly detrimental to health.

All of these tendencies cannot be interpreted as being other than of a decidedly harmful nature. Another effect which the administration of the sulphur produced, and one of a more serious character still, is found in the impoverishment of the blood in respect of the number of red and white corpuscles therein. The administration

of a substance which diminishes by a notable percentage these important component particles of the blood must be regarded in every sense as highly prejudicial to health. Some of the most important functions of the blood, as has been well established by careful physiological studies, are intimately connected with the number and activity of both the red and white corpuscles. The bleaching effect of the sulphurous acid upon the color of the blood is a matter of less consequence and no great effect is produced upon the hemoglobin, but the diminution of the number of red and white corpuscles is a matter of serious concern.

The variations of the metabolic processes from the normal, as indicated in this series of experiments, were never of a character favorable to a more healthy condition of the system, but, on the other hand, all these variations, in so far as the effect of the changes could be distinguished, are of a prejudicial character. There is no evidence whatever that the sulphur added to the foods in the form of sulphurous acid, or sulphites, takes any part in the nutrition of the tissues of the body containing sulphur, namely, the proteids; hence, no claim of food value can be established for these bodies. The evidence all points to the fact that they are purely drugs, devoid of food value, having no favorable effects upon the metabolic processes, but, on the other hand, exerting deleterious and harmful effects. The conclusion, therefore, is inevitable that, as a whole, the changes produced in metabolic activity by the administration of sulphur in the forms noted above in the comparatively short time covered by the experiments are decidedly injurious.

The verdict which must be pronounced in this case is decidedly unfavorable to the use of this preservative in any quantity or for any period of time, and shows the desirability of avoiding the addition of any form of sulphurous acid to products intended for human food.

Benzoic Acid and Benzoates.—From a careful study of the data in the individual cases and of the summaries of the results, it is evident that the administration of benzoic acid, either as such or in the form of benzoate of soda, is highly objectionable and produces a very serious disturbance of the metabolic functions, attended with injury to digestion and health.

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As in the case of boric acid, salicylic acid, and sulphurous acid, this injury manifests itself in a number of different ways, both in the production of unfavorable symptoms and in the disturbance of metabolism. These injurious effects are evident in the medical and clinical data which show grave disturbances of digestion, attended by phenomena which are clearly indicative of irritation, nausea, headache, and in a few cases vomiting. These symptoms were not only well marked, but they were produced upon healthy individuals receiving good and nourishing food and living under proper sanitary conditions. It is only fair to conclude, therefore, that under similar conditions of administration of benzoic acid or benzoate of soda in the case of weaker systems, or less resistant conditions of health, much more serious and lasting injury would be produced.

It was also noticed that the administration of benzoic acid and benzoate of soda was attended with a distinct loss of weight, indicative of either a disturbance of assimilation or an increased activity in those processes of the body which result in destruction of tissue. The production of a loss of weight in cases of this kind must be regarded as indicative of injurious effects.

The influence of the benzoic acid and benzoate of soda upon metabolism was never of a character indicative of a favorable change therein. While often the metabolic changes were not strongly marked, such changes as were established were of an injurious nature. It is evident that the administration of these bodies, therefore, in the food tends to derange metabolism in an injurious way.

An important fact in connection with the administration of these bodies is found in the efforts which nature makes to eliminate them from the system. In so far as possible the benzoic acid is converted into hippuric acid. There is a tendency usually manifested, however, to retain the benzoic acid in the body for a notable length of time, and this is much more marked in the case of benzoate of soda than in the case of benzoic acid.

While the administration of both these bodies, therefore, is undoubtedly harmful, the injurious effects are produced more rapidly in the case of benzoic acid than they are in the case of benzoate of soda; the data, however, will show that the total harmful effect produced in the end is practically the same in both cases, hence there

appears to be no reason for supposing that the administration of the preservative in the form of benzoate of soda can be justified by any argument relating to the less injurious effect thereof upon health.

The occurrence of microscopic bodies in the urine is undoubtedly increased under the administration of benzoic acid in all its forms, thus showing conclusively the tendency to stimulate the destructive activities of the body.

Coming to the final consideration of all these different phases of the subject, there is only one conclusion to be drawn from the data which have been presented and that is that in the interests of health both benzoic acid and benzoate of soda should be excluded from food products. This conclusion is reached independently of any consideration of the conditions which it is alleged surround the processes of manufacture and which result in the demands of manufacturers to be allowed to continue the use of this body. This is a subject which must be discussed from an entirely different point of view and has no bearing whatever upon the general conclusions which have been reached, namely, that both benzoic acid and benzoate of soda are bodies which, when added to foods, are injurious to health.

Formaldehyde.—A general study of all the data leads to the conclusion that the admixture of formaldehyde with food is injurious to health, even in the case of healthy young men. It is fair to conclude, therefore, that in the case of infants and children the deleterious effects would be more pronounced. The metabolic functions are disturbed in a notable way, both by the retardation of the nitrogen and sulphur metabolism, and the acceleration of phosphorus metabolism. There seems to be a tendency to an increased absorption from the alimentary canal, especially in the cases when the formaldehyde had stood in contact with the milk, and hence it is fair to presume that in so far as the enzymic action in the intestinal canal is concerned, transforming solid food into soluble materials which may enter the circulation, there is evidently a stimulating effect produced.

There are, however, many varying conditions which must be considered in properly interpreting the data. The uniformly increased absorption of the proteid elements of the food, and also of

the sulphur and phosphoric acid, accompanied in the first two instances by a decrease in the metabolized elements excreted and in the last instance, namely, phosphoric acid, by a pronounced increase in metabolism, makes the explanation of the data rather difficult. Attention should be called to the fact that while the variations from normal metabolism are not very wide, the individual data are remarkably uniform and consistent.

The conditions which are noted in the case of the proteins would lead one to expect a gain in the body weight. This expectation, however, is not realized for either class of subjects, although the losses in weight are so slight as to be practically negligible. The ratio of the food weight to the body weight was uniformly maintained throughout the experiment, and, hence, if no variations in metabolic activity had occurred a fair presumption would have been that the body weight would remain constant. That the change of weight was slight in the view of the disturbances of the metabolic functions may be accounted for by the inhibiting or retarding influence of the preservative upon the nitrogen and sulphur katabolism, or by the slight increase in water in the urine and feces. It cannot be maintained, however, that a retarded katabolism is beneficial to health. On the contrary a more rapid renewal of the tissues within the limits of healthy activity would be more likely to preserve a normal condition. The old tissues cannot be expected to functionate as perfectly as those which are newer, and hence, within reasonable limits, a change of the tissues of the body must be considered as necessary to a healthy condition, and the maintenance of a normal vitality.

The medical data indicate plainly that formaldehyde, even when given in small quantities, is an irritating substance to the mucous membrane, and, therefore, the normal organs are at first actively stimulated to rid themselves of the irritating foreign substance. It is not strange, therefore, that this preservative had a marked stimulative action on those organs and cells secreting the various digestive juices. It is evident that when the digestive and excretory organs of the body are excited to unusual activity by such an extraneous body having neither food nor condimental value, they act in self defence, and it would be wholly illogical to conclude from

this increased excitation that these bodies were helpful to digestion and conducive to health. The nature of the investigation made it impossible to determine whether any organic change took place in the various organs affected, but it may be assumed that any such change which these organs had undergone in the limited time was not sufficient to disturb in any notable way their normal functions which they would perform until the continued administration of the drug produced disease due to the excessive stimulation.

In the case of phosphoric acid, the increased katabolic activity is difficult of definite interpretation, though it is established beyond doubt that such an effect is produced. The formaldehyde may exert a selective action for those proteid bodies high in phosphorus, rendering them insoluble, but in this case there would be an excess of phosphorus in the feces, which is not found. Or the formaldehyde may induce a change in the process of digestion whereby the phosphorus of the food is changed into a soluble and easily excreted form without passing through the tissues of the body. This might easily be the case if in the process of digestion the glycerol-phosphoric acid formed is transformed into soluble inorganic salts, which are readily excreted. Whatever may be the explanation, the changes indicated in normal metabolism, accompanied as they are by the development of the symptoms described, can only be considered as prejudicial to health.

The general tendency to produce a slight decrease in the temperature of the body, assuming for the moment that the data warrant the conclusion that such a condition of affairs existed, might well be due to the inhibition of cell activity shown by the retardation in the breaking down of tissues. The normal functions of the body would doubtless be disturbed by such a condition, aside from the irritating and other disturbing influences exerted by the exhibited drug.

The tendency of the preservative to produce albumin in the urine, while not well marked, is at least worthy of attention. The fact that only slight changes take place in the body weight is sufficiently explained in the data and cannot be urged in favor of the exhibited preservative.

Apart from the injurious effects of formaldehyde itself, its use

as a food preservative would be especially inadvisable in milk or cream, because its addition in dilute solution prevents the growth of acid-forming bacteria, but has no effect in retarding the action of many harmful organisms; in other words, the milk is prevented from becoming sour and thus indicating its age and the danger signal is thus removed, while the other organisms which are capable of producing disease continue to multiply in the milk with practically the same degree of rapidity as if the formaldehyde was not present.

The final conclusion, therefore, is that the addition of formaldehyde to foods tends to derange metabolism, disturb the normal functions, produce irritation and undue stimulation of the secretory activities, and, therefore, it is never justifiable.

Sulphate of Copper.—The data which have been collected in the course of this experiment have led to the conclusion that the administration of sulphate of copper even in the extremely small quantities in which it has been given has a very distinctly unfavorable effect upon health and digestion, as indicated by the ordinary clinical and medical summaries. Severe pains are produced in the stomach accompanied often with nausea and sometimes with vomiting, there is a general tendency to malaise, often a development of headache, and other unfavorable symptoms of a more or less persistent and uniform character. Further than this, the symptoms which are usually not developed for about a week continue in some instances for a number of days into the after-period after the sulphate of copper has been withdrawn. The data indicate that copper, like many other metals, is likely to produce a cumulative effect, and that its administration in even much smaller quantities than those indicated, or less than those which would be ingested in the regular consumption of coppered vegetables, is attended with more or less danger on this account.

There was a very small loss of weight in nine of the subjects, while the three who showed the greatest tolerance of the copper sulphate gained in weight. No definite conclusions can, therefore, be formed respecting the general effect upon the weight of the body, except that in the cases where uniform effects are produced there is a slight loss of weight.

The copper salt which was used in this experiment differs from

other chemicals which have been used in this series of investigations in that its excretion falls only partly upon the kidneys. The effect produced on the urine, therefore, cannot be ascribed directly to the copper salt employed, but only to such derangements of the metabolism due thereto as would incidentally affect the composition of the urine.

The effect upon the general metabolism is of a character which, though not very pronounced, is indicative of a retardation of normal metabolic processes. Inasmuch as a small quantity of sulphur was introduced into the system through the copper salt, the quantity of this sulphur must be taken into consideration in studying the effect on metabolism. There is seen to be quite a uniform tendency to derange the ratio of the metabolized sulphur and nitrogen.

The apparent increase in the relative quantities of sulphur excreted is due rather to the diminution in the nitrogen than to an actual increase in the sulphur over that which would be expected from the ingestion of the sulphuric acid in the copper salt. The most marked change in the sulphur compounds is in the case of neutral sulphur, which shows a decided and uniform increase during the administration of the copper salt and in some cases for several days thereafter.

The effect produced upon the metabolism of nitrogen is more important. Under the administration of sulphate of copper there is a marked and constant decrease in the excretion of urea, which is a matter of great significance. Such a decrease can only be regarded as an indication of a retarding effect on nitrogen metabolism. At the same time the quantity of uric acid and xanthin bases are increased during the administration of the copper salt and the increase in xanthin is still very marked in the after-period. These two important observations indicate that the nitrogen metabolism is disturbed in a way which must be considered injurious to health.

There is also a notable effect produced upon the phosphoric acid metabolism. There is a marked decrease in the total metabolized phosphorus, and, while the non-metabolized phosphorus is less uniformly affected, there is a decided tendency shown to decrease the

total excretion of phosphoric acid under the influence of the copper sulphate.

The final conclusion, based on the medical and clinical data and on the study of the effect of the copper sulphate upon metabolism, is that the administration of this salt is prejudicial to health.

Potassium Nitrate.—It is evident that the administration of small quantities of potassium nitrate induce only slight disturbances in the metabolic processes, and indicate only to a slight degree harmful or deleterious effects as noted in the medical and clinical data. It is evident moreover that with the exception of one instance, namely, the increase of the number of red corpuscles in the blood, that no beneficial effect can possibly be attributed to the exhibition of this chemical.

While the data are in this case far less conclusive than those in any of the preceding cases, they are of a character to warrant the suggestion that so far as health and digestion are concerned it is safer to omit a body of this kind from the food. There are some foods which naturally contain small quantities of potassium nitrate. Its very poisonous action when taken in large doses, however, is a warning which should cause great care in its use even in small quantities and deter any one charged with the protection of the public health from expressing any favorable opinion in respect to its use.

It is evident that potassium nitrate in the quantities used has neither a preserving effect nor has it any condimental value. Whatever may be said to the contrary, it is perfectly evident that the sole purpose of its use is the intensification of the red color of meats after preservation. Whatever may be the ethical principle underlying this use of potassium nitrate is a question which is not the subject of discussion in a bulletin of this kind, but it is only due to the consumer that the real purpose of using potassium nitrate in the curing of meats should be revealed.

The further question arises as to whether or not the coloring of preserved meats in this way in order that they may have the color of fresh meats is a violation of the Food and Drugs Act, which forbids the coloring of food products for the purpose of concealing damage or inferiority.

While, therefore, the data which have been accumulated are not such as to warrant a sweeping condemnation of potassium nitrate in foods, they are sufficiently indicative to justify the conclusion that its presence in foods is undesirable and open to suspicion.

General Considerations.

Having thus set forth the general results of this long and laborious study, it is seen that if the conclusions based upon the experimental data are correct that there can be no justification of the process of adding chemical preservatives to human foods. Successful manufacturing establishments have demonstrated beyond peradventure that better, more wholesome, and more permanent forms of food products can be produced without the aid of any preservative whatever. Sterilization will preserve sweet cider better than benzoate of soda. Proper care in handling fruits and in conducting the manufacturing processes for preserves, jams and marmalades will make a more palatable product and one that keeps better than the use of salicylic acid. Careful curing of meats and proper care in transportation will preserve these meats better than boric acid. The natural color of the pea kept in a sanitary can where its color is not lost by action due to imperfections of the tin will make a far more palatable article than will the use of sulphate of copper, and so on to the end of the list. There is no single food product which is not more palatable and of equal if not better keeping qualities when made carefully without the use of preservatives. There is, therefore, absolutely no commercial necessity for the use of these bodies, but it is urged by those who employ them that even though considerable quantities of these bodies are injurious to the health, which no one denies, yet in the minute quantities in which they are used in foods they can not be regarded as in any way deleterious. It is easy to show that such an opinion is without scientific basis. It is quite impossible for any expert who holds this opinion to indicate to any jury, much more to the great jury of the American people any point in the addition of the preservative to food at which it remains harmless, or the point at which it begins to be harmful. Unless such a point could be fixed and demonstrated upon reliable

experimental data, it is evident that no scientific reason can be urged for the use of limited quantities of a preservative, which is acknowledged to be harmful, on the ground that in such quantities it is not injurious.

Inasmuch as a preservative is not a food, and as it does not in any way take part in the nourishment of the body nor in the restoration of waste or growth; and further as it is necessarily eliminated, either unchanged or in other forms which may be even more harmful than the original, by the excretory organs of the body, thus imposing upon them an unnecessary and injurious burden and affecting more or less the constitution of the ultimate cells thereof in an unfavorable way, it is evident that the argument which would permit their use in small quantities is wholly illegitimate.

The fallacy of the argument that small quantities of an injurious substance are not injurious may perhaps be best represented graphically. The chart which accompanies this discussion shows theoretically the normal and lethal dose of a food and a drug or, as in this case, a chemical preservative. The chart shows two curves, one representing a chemical preservative and one representing a food. The normal dose of a food is that quantity of food which maintains a healthy adult body in equilibrium. It is represented on the right of the chart by the number 100. If the quantity of food necessary to maintain the equilibrium in a healthy adult body is slightly diminished, no apparent change is at first experienced and possibly even no discomfort. If, however, the quantity of food be still further diminished progressively, as indicated by following the curve down to the left, the point is finally reached when no food is given at all and death ensues, represented by zero on the left hand of the diagram designated "lethal dose." As the curve begins to deviate from the perpendicular on the right the degree of injury is very readily noticed and starvation or symptoms of starvation are set up. Thus, if you follow the perpendicular on the right downward to the point 80, the divergence of the corresponding point of the curve is already measurable. As you descend to zero the magnitude of the measurement increases. It requires but very little further illustration to show how easily the effect of diminishing the normal dose of

a food can be measured immediately after the curve begins to vary appreciably from the perpendicular on the right.

Let us now consider the perpendicular on the left, which is marked at the top under the term "lethal dose," viz.; a quantity of the added preservative sufficient to destroy life. The normal dose of such an added chemical preservative is 0, and is shown at the base line to the right marked "normal dose." If you add a very minute quantity of a chemical preservative, the curve representing it varies

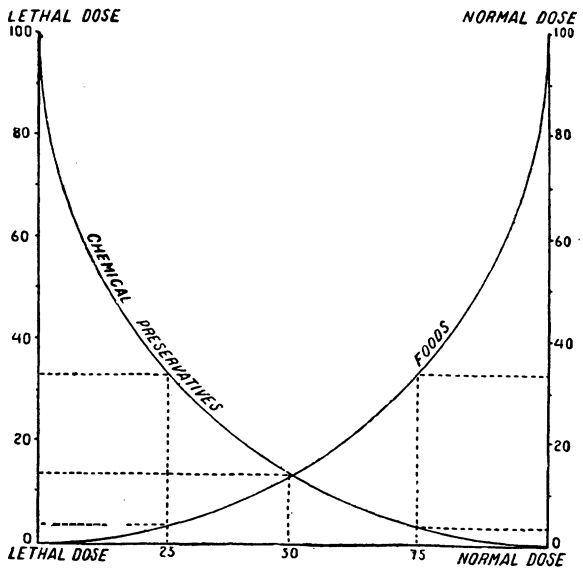

FIG. 1. Graphic chart representing the comparative influences of foods and preservatives.

so slightly from the horizontal base as to be impossible of measurement by ordinary means. If we follow along to the number 75, on the horizontal base, we see the deviation of the curve is sufficiently great to measure. At 50 it is still greater, at 25 still greater, while at the left of the basic line it is a maximum, extending from 0 to 100, or the lethal dose. It is easy to show by mathematical data that no matter how small the quantity of an injurious substance or preservative is, it will still produce an injurious effect, which may be infinitely small if the dose be infinitely small. It follows then, as a

mathematical demonstration, that any quantity of an injurious substance added to a food product must of necessity be injurious, provided it is in the nature of a drug and the body is in a perfectly healthy normal condition.

Hence the argument which has been so persistently urged in favor of a chemical preservative that if in small quantities it is harmless is shown to be wholly untenable. Where there is no necessity for the addition of a harmful substance, where no particular benefit is secured thereby, and where there is no disturbance of the normal state of health there can be no possible excuse of a valid nature to offer for the exhibition of even minute quantities. That these minute quantities would not be dangerous, in so far as producing any fatal effect is concerned, is conceded, but that, in the end, they do not produce any injury, even in these small quantities, is certainly to be denied.

The course of safety, therefore, in all these cases is to guard the opening of the door. If the use of small quantities is permitted, then there can never be any agreement among experts or others respecting the magnitude of the "small quantity," and continued litigation and disagreement must follow. On the other hand, when the harmfulness of any substance which it is proposed to add to food is established and no reason for its use can be given other than the convenience, carelessness, or indifference of the manufacturer, the exclusion of such bodies entirely from food products follows as a logical sequence and a hygienic necessity.